DUKE UNIVERSITY MEDICAL CENTER

Department of Surgery
Surgical Virology Laboratory

March 4, 1985

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University of California, SF
San Francisco, CA

Dear Harold:

It was good to have the opportunity to talk with you about how to approach an appropriate nomenclature system for the human retroviruses. I am sure that you are wondering about what kind of manipulation you are being subjected to, so let me address that issue first. There is certainly no mystery about my friendship with Bob Gallo and therefore its unreasonable to think that I can ignore his influence in all of this. You must realize, however, that what Bob needs most is sound advice from independent thought and if I'm to have a role in this game that is what I would like it to be. Parenthetically, it was at Bob's suggestion that I call you about your advice as to how best to proceed with this.

What I would like to do in this letter is to outline my perceptions of the salient features of the problem. This is not to be interpreted as a pitch for any specific designation at this point, although it may appear as such. Let me first address the issue of HTLV-III in a historical perspective. In November of 1983, a nomenclature meeting was held at Cold Spring Harbor consisting of U.S., Japanese and European scientists. An agreement was reached to designate HTLV's as human T lymphotropic retroviruses and assign successive roman numerals to new isolates. Gallo obviously followed this course and for a period of time as did the Pasteur group. However, the designations changed rapidly in France, first to IDAV, then to LAV. Subsequently, the San Francisco isolate, ARV, was reported. You indicated that now that the sequences are known, the historical perspective may be irrelevant because on that basis we appear to be dealing with a new class of retroviruses. I would question, however, whether the sequence data should be the primary guide for appropriately naming this virus. Other characteristics should be weighted in this regard and it is here where your committee should do its homework carefully. In the tables which I've attached, some of the common and distinguishing features of the human retrovirus isolates are listed. There may be others and some can be debated, but it appears to me to be a reasonable way to begin.

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Let me address the issue of what to call these viruses. In my opinion, both LAV and ARV are inappropriate. People can have lymphadenopathy without the virus or the virus without lymphadenopathy. ARV presents an even greater problem. Telling a patient he has the AIDS virus is like sounding a death knell. Its true that the word "related" qualifies it somewhat for the scientist but in practice it presents a real problem to clinicians, and this has been voiced repeatedly.

I'm not sure if I have a better name than any of the above. I would offer some of my own thoughts nonetheless. One could include all human retroviruses in a family called HRV (human retroviruses). For those whose primary target is the T cell, designate these HTRV (human T lymphotropic retroviruses). These could be subdivided according to diseases spectrum if this is desirable. For instance, those associated with adult T-cell leukemia might be designated HTRV (ATL). For the new class I would propose HTRV (Immunodeficiency or ID) and follow this with a notation for the principle isolate, i.e.

HTRV (ID) - Paris

HTRV (ID) - Bethesda

HTRV (ID) - San Francisco

The major stumbling block I have in separating the ATL from the ID agents is the little known fact that the ATL related viruses also cause ID. This has been repeatedly documented in vitro and there are published reports that with HTLV-I is associated with immunodeficiency in certain disease groups. Bear in mind that what these viruses manifest is not an acute immunodeficiency, but a more subtle phenomenon whose consequences are more difficult to trace, although nonetheless very important. In this context, the new virus class may do the very same thing in some infected individuals which don't develop frank AIDS but nevertheless succumb to other diseases. We also don't have a clue as to what will happen to the thousands of infected individuals who have not yet developed disease. It is here where I find Bob's argument not to separate these agents by name very difficult to resist. In this context, human T lymphotropic retroviruses is an eminently sensible designation.

Nonetheless, I agree with you that Bob ought to take the lead and be as flexible as possible about the name of the virus. I'm sure he will call you to discuss this soon.

Please let me know your thoughts and if I can help further in this matter. I also take this opportunity to include some pseudoscience and responses which highlight the need to quickly do something about this.

With best regards,

Yours sincerely,

Dani P. Bolognesi

DPB/ke

Enclosures

RELATEDNESS OF HTLV-III/LAV TO HTLV-I and -II

1. Lymphotropism

*2. Particular T-4 Tropism

3. In Vitro Induction of Syncytial Formation

4. In Vitro and In Vivo Impairment of T-Cell Function

5. Relatively small major core protein (p24/25)

*6. P24 juxtaposed to NH2-terminal gag protein, i.e., no phosphoprotein in this position.

*7. Common P24/25 epitope with both heterologous (rabbit) antisera and a human monoclonal antibody.

*8. Common envelope protein epitope?

*9. Double splice to generate 3' mRNA of about 2Kb.

*10. Transacting transcriptional activation.

11. Stretch of nucleotide sequence homology gag - pol region of LTRs.

*Indicates unique features of HTLV-I, II, III.

UNIQUE FEATURES OF HTLV-III/LAV IN RELATION TO HTLV-I AND -II

1. Morphology

2. Overall Sequence Homology

3. Organization of Coding Regions

4. Envelope Polymorphism

5. Degree of <u>In Vivo</u>, <u>In Vitro</u> Cytopathic Effects on T_4 Cells